```
=> RDRP
L1          897 RDRP

=> virus
L2      1082335 VIRUS

=> L1 and L2
L3          810 L1 AND L2

=> screening
L4       326272 SCREENING

=> L3 and L4
L5           29 L3 AND L4

=> D L5 IBIB ABS 1-29
```

=> H"HCV replicon"
L6 0 H"HCV REPLICON"

=> "HCV replicon"
L7 325 "HCV REPLICON"

=> "RdRp"
L8 897 "RDRP"

=> L7 and 18
L9 23 L7 AND L8

=> screening and L9
L10 1 SCREENING AND L9

=> D L10 IBIB ABS

L10 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:261230 CAPLUS
TITLE: Purification and characterization of HCV RNA-dependent RNA polymerase from Korean genotype 1b isolate: implications for discovery of HCV polymerase inhibitors
AUTHOR(S): Kim, Jeongmin; Lee, Mikyoung; Kim, Yong-Zu
CORPORATE SOURCE: Drug Discovery, LG Life Sciences, Ltd., Daejeon, 305-380, S. Korea
SOURCE: Bulletin of the Korean Chemical Society (2005), 26(2), 285-291
CODEN: BKCSDE; ISSN: 0253-2964
PUBLISHER: Korean Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The nonstructural protein 5B (NS5B) of hepatitis C virus (HCV) is the viral RNA-dependent RNA polymerase (**RdRp**), which is the essential catalytic enzyme for the viral replication and is an appealing target for the development of new therapeutic agents against HCV infection. A small amount of serum from a single patient with hepatitis C was used to get the genome of a Korean HCV isolate. Sequence anal. of NS5B 1701 nucleotides showed the genotype of a Korean isolate to be subtype 1b. The soluble recombinant HCV NS5B polymerase lacking the C-terminal 24 amino acids was expressed and purified to homogeneity. With the highly purified NS5B protein, we established in vitro systems for **RdRp** activity to identify potential polymerase inhibitors. The rhodanine family compds. were found to be potent and specific inhibitors of NS5B from high throughput **screening** (HTS) assay utilizing the scintillation proximity assay (SPA) system. The binding mode of an inhibitor was analyzed by measuring various kinetic parameters. Lineweaver-Burk plots of the inhibitor suggested it binds not to the active site of NS5B polymerase, but to an allosteric site of the enzyme. The activity of NS5B in in vitro polymerase reactions with homopolymeric RNA requires interaction with multiple substrates that include a template/primer and ribonucleotide triphosphate. Steady-state kinetic parameter, such as Km, was determined for the ribonucleotide triphosphate. One of compds. found interacts directly with the viral polymerase and inhibits RNA synthesis in a manner noncompetitively with respect to UTP. Furthermore, we also investigated the ability of the compound to inhibit NS5B-directed viral RNA replication using the Huh7 cell-based **HCV replicon** system. The investigation is potentially very useful for the utility of such compds. as anti-hepatitic agents.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D L9 IBIB ABS 1-23

L9 ANSWER 1 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN

L5 ANSWER 9 OF 29 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:770086 CAPLUS
DOCUMENT NUMBER: 137:290923
TITLE: Recombinant hepatitis C **virus** RNA replicase expressed in E. coli and BHK cell and its use in HCV infection diagnosis and antiviral drug **screening**
INVENTOR(S): Hagedorn, Curt H.
PATENT ASSIGNEE(S): Emory University, USA
SOURCE: U.S., 35 pp., Cont.-in-part of U.S. 6,248,589.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 6461845	B1	20021008	US 2000-597877		20000620
US 5981247	A	19991109	US 1996-722806		19960927
US 6248589	B1	20010619	US 1999-337028		19990625
US 2003152915	A1	20030814	US 2002-241872		20020912
PRIORITY APPLN. INFO.:			US 1995-4383P	P	19950927
			US 1996-722806	A3	19960927
			US 1999-337028	A2	19990625
			US 2000-597877	A3	20000620

AB A recombinant RNA-dependent RNA polymerase of hepatitis C **virus** (r-HCV-**RDRP**) coding DNA was cloned and expressed in Escherichia coli or mammalian BHK cells yielding active enzyme in vitro. The r-HCV-**RDRP** can include up to 20 added amino acids and up to nine deleted or substituted amino acids at the NH2-terminus of the encoded amino acid sequence. The cDNA for HCV NS5B region with min. changes at the N-terminus is PCR amplified and directionally cloned into pET-11a. The recombinant protein contain MASMSY at the N-terminus rather than the SMSY N-terminus of wild-type NS5B protein. The enhance the enzymic activity, the r-HCV-**RDRP** can be further modified to contain some amino acid substitutions, including Ser or Glu at amino acid position 21, Arg or Lys at amino acid position 67, Lys at amino acid position 100, Lys at amino acid position 116, Glu or Val at amino acid position 133, Ser at amino acid position 220, Ser at amino acid 302, or Ala at amino acid position 340. In addition, the 55-amino acid carboxy terminal region can also be deleted and replaced with LeuGlu(His)6 or. The invention provides method to solubilize r-HCV-**RDRP** from a host cell lysate and purified r-HCV-**RDRP**. Methods for **screening** for inhibitors of r-HCV-**RDRP** in vitro, for making stably transfected mammalian cells expressing r-HCV-**RDRP** and for in vivo testing of r-HCV-**RDRP** inhibitors in vivo are disclosed. The invention provides antibodies to r-HCV-**RDRP** and methods for detecting antibodies to HCV-**RDRP** in serum of human patients.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THI

L5 ANSWER 13 OF 29 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:816893 CAPLUS
DOCUMENT NUMBER: 135:353893
TITLE: Internal de novo initiation sites of the NS5B RNA dependent RNA polymerase of hepatitis C **virus** NS5B and uses thereof
INVENTOR(S): Pellerin, Charles; Kukolj, George
PATENT ASSIGNEE(S): Boehringer Ingelheim (Canada) Ltd., Can.
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001083736	A2	20011108	WO 2001-CA580	20010420
WO 2001083736	A3	20020801		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001055756	A1	20011227	US 2001-838386	20010420
EP 1278837	A2	20030129	EP 2001-927534	20010420
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-198793P P 20000421
WO 2001-CA580 W 20010420

AB The present invention provides a de novo initiation site comprising a polypyrimidine tract having a cytidylate nucleotide or a polycytidylate (poly C) cluster located therein or adjacent thereto. This site provides a RNA template for assessing in vitro RNA dependent RNA polymerase (**RdRp**) activity of flavivirus. Particularly, the invention relates to de novo initiation sites of the NS5B protein of the hepatitis C **virus** and methods for identifying specific inhibitors thereof. To further define the nature of de novo initiation from the 3'-UTR, several distinct 3'-UTR's that harbor the conserved terminal 98 nucleotides, but have poly U/U-C tracts of different length were isolated and characterized. Reconstitution of de novo initiation by the mature NS5B with the different 3'-UTR RNA substrates revealed distinctively sized products that are consistent with internal initiation at specific sites within the polypyrimidine tract. These sites were mapped by demonstrating that nucleotide substitutions of the cytidylate residues in the poly U/U-C template affect the generation of specific products of the de novo initiation reaction. Moreover, initiation within the poly U/U-C template is also primed by GTP and an assay that evaluates inhibitors of this reaction as potential HCV therapeutics is claimed

L5 ANSWER 14 OF 29 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:475828 CAPLUS
DOCUMENT NUMBER: 133:115871
TITLE: Uses of flavivirus RNA-dependent RNA polymerases (**RdRp**) in viral infection diagnosis and anti-viral drug **screening**
INVENTOR(S): Kao, C. Cheng
PATENT ASSIGNEE(S): Advanced Research and Technology Institute, Inc., USA
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000040759	A2	20000713	WO 2000-US152	20000105
WO 2000040759	A3	20001123		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:		
US 1999-114779P	P	19990105
US 1999-474847	A	19991230

AB An isolated viral RNA-dependent RNA polymerase (**RdRp**) is provided that is useful in diagnostic applications to amplify nucleic acids. The **RdRps** from flavivirridae families including flavivirus, BVDV (bovine viral diarrhea **virus**) and HCV (hepatitis C **virus**) and an alphavirus-like plant **virus** BMV (brome mosaic **virus**) can initiate de novo RNA synthesis from the terminus of either RNA or DNA template. RNA synthesis initiation requirements (such as detailed characterization of the promoter sequences directing subgenomic and genomic RNA synthesis and nucleotide modification effect) of BMV **RdRp** and BVDV **RdRp** (NS5B) are very similar. The establishment of the conditions for flavivirus **RdRp** RNA synthesis may lead to the development of test kits for viral infection diagnosis and anti-viral drug **screening**

L5 ANSWER 17 OF 29 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:324407 CAPLUS
DOCUMENT NUMBER: 126:289023
TITLE: Cloning of recombinant hepatitis C **virus** RNA replicase in Escherichia coli and mammalian cells
INVENTOR(S): Hagedorn, Curt H.; Al, Reinoldus H.
PATENT ASSIGNEE(S): Emory University, USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9712033	A1	19970403	WO 1996-US15571	19960927
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2233309	AA	19970403	CA 1996-2233309	19960927
AU 9672007	A1	19970417	AU 1996-72007	19960927
AU 719122	B2	20000504		
EP 859833	A1	19980826	EP 1996-933178	19960927
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11514862	T2	19991221	JP 1996-513707	19960927
PRIORITY APPLN. INFO.:			US 1995-4383P P	19950927
			WO 1996-US15571 W	19960927

AB A cDNA encoding recombinant RNA-dependent RNA polymerase of hepatitis C **virus** (r-HCV-**RDRP**) was cloned and expressed in Escherichia coli or mammalian BHK cells yielding active enzyme in vitro. The r-HCV-**RDRP** can include up to 20 added amino acids and up to 9 deleted or substituted amino acids at the N-terminus of the encoded amino acid sequence. Thus, PCR primers were designed for the amplification of the NS5B region of the hepatitis C **virus** with min. changes at the N-terminus, and the cDNA directionally cloned into pET-11a. This construct results in the synthesis of a recombinant protein with an N-terminal sequence of MASMSY rather than the SMSY N-terminus of wild-type NS5B protein. Methods to solubilize and purify r-HCV-**RDRP** from a host cell lysate are also provided. Methods for **screening** for inhibitors of r-HCV-**RDRP** in vitro, for making stably transfected mammalian cells expressing r-HCV-**RDRP**, and for in vivo testing of r-HCV-**RDRP** inhibitors in vivo are disclosed. Antibodies to r-HCV-**RDRP** and methods for detecting antibodies to HCV-**RDRP** in serum of human patients are described. A reporter system was devised whereby activity of r-HCV-**RDRP** expressed in a host cell is required for expression of a reporter gene; the host cell is transfected with a construct designed to carry the reporter coding sequence in antisense form in a structure that models the HCV replicative intermediate when expressed as mRNA.

L5 ANSWER 20 OF 29 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:186166 BIOSIS
DOCUMENT NUMBER: PREV200400190599
TITLE: In vitro system for replication of RNA-dependent RNA polymerase (**RDRP**) **viruses**.
AUTHOR(S): King, Robert W. [Inventor, Reprint Author]; Jeffries, Matthew W. [Inventor]; Pasquinelli, Claudio [Inventor]
CORPORATE SOURCE: West Chester, PA, USA
ASSIGNEE: Bristol-Myers Squibb Company
PATENT INFORMATION: US 6699657 20040302
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Mar 2 2004) Vol. 1280, No. 1. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Apr 2004
Last Updated on STN: 7 Apr 2004

AB An in vitro method to conduct genomic replication of the viral genomes of **viruses** that utilize RNA-dependent RNA polymerase for replication (**RDRP viruses**), such as HCV. The method employs a construct comprising the 3' and 5' untranslated regions (UTRs) of the viral genome which are operably linked on the 5' and 3' ends of a reporter sequence, in antisense orientation, such that when viral replication is occurring within the cell which produces **RDRP**, the reporter protein will be made. The method of the invention provides an efficient means for measuring genomic replication in **RDRP viruses** , and also for the rapid **screening** of compounds for their ability to inhibit genomic replication of **RDRP viruses** , including the Hepatitis C **virus** (HCV).

L5 ANSWER 24 OF 29 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:611091 BIOSIS
DOCUMENT NUMBER: PREV200200611091
TITLE: Recombinant hepatitis C **virus** RNA replicase.
AUTHOR(S): Hagedorn, Curt H. [Inventor, Reprint author]
CORPORATE SOURCE: Atlanta, GA, USA
ASSIGNEE: Emory University
PATENT INFORMATION: US 6461845 20021008
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Oct. 8, 2002) Vol. 1263, No. 2. http://www.uspto.gov/web/menu/patdata.html. e-file. CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Nov 2002
Last Updated on STN: 27 Nov 2002

AB A recombinant RNA-dependent RNA polymerase of hepatitis C **virus** (r-HCV-**RDRP**) coding DNA was cloned and expressed yielding active enzyme in vitro. The r-HCV-**RDRP** can include up to 20 added amino acids and up to nine deleted or substituted amino acids at the NH2 -terminus of the encoded amino acid sequence. The invention provides method to solubilize r-HCV-**RDRP** from a host cell lysate and purified r-HCV-**RDRP**. Methods for **screening** for inhibitors of r-HCV-**RDRP** in vitro, for making stably transfected mammalian cells expressing r-HCV-**RDRP** and for in vivo testing of r-HCV-**RDRP** inhibitors in vivo are disclosed. The invention provides antibodies to r-HCV-**RDRP** and methods for detecting antibodies to HCV-**RDRP** in serum of human patients.

L5 ANSWER 26 OF 29 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:278466 BIOSIS
DOCUMENT NUMBER: PREV200000278466
TITLE: Recombinant hepatitis C **virus** RNA replicase.
AUTHOR(S): Hagedorn, Curt H. [Inventor, Reprint author]; Al, Reinoldus H. [Inventor]
CORPORATE SOURCE: Atlanta, GA, USA
ASSIGNEE: Emory University, Atlanta, GA, USA
PATENT INFORMATION: US 5981247 19991109
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Nov. 9, 1999) Vol. 1228, No. 2. e-file. CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Jul 2000
Last Updated on STN: 7 Jan 2002

AB A recombinant RNA-dependent RNA polymerase of hepatitis C **virus** (r-HCV-**RDRP**) coding DNA was cloned and expressed yielding active enzyme in vitro. The r-HCV-**RDRP** can include up to 20 added amino acids and up to nine deleted or substituted amino acids at the NH2 -terminus of the encoded amino acid sequence. The invention provides method to solubilize r-HCV-**RDRP** from a host cell lysate and purified r-HCV-**RDRP**. Methods for **screening** for inhibitors of r-HCV-**RDRP** in vitro, for making stably transfected mammalian cells expressing r-HCV-**RDRP** and for in vivo testing of r-HCV-**RDRP** inhibitors in vivo are disclosed. The invention provides antibodies to r-HCV-**RDRP** and methods for detecting antibodies to HCV-**RDRP** in serum of human patients.

L5 ANSWER 27 OF 29 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:189879 BIOSIS